THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

_____

Ex parte GANESH M. KISHORE, DAVID A. EICHHOLTZ and CHARLES S. GASSER

_____

Appeal No. 93-2460
Application 07/590,647[1]

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ON BRIEF

_____

Before WILLIAM F. SMITH, GRON, and ELLIS, ***Administrative Patent Judges***.

ELLIS, ***Administrative Patent Judge.***

DECISION ON APPEAL

This an appeal from the final rejection of claims 1 through 48. Claims 49 through 54 are also pending, but have been withdrawn from consideration by the examiner under 37 CFR § 1.142(b).

[1] Application for patent filed September 28, 1990.

We initially note the appellants' statement that the claims stand or fall together. Brief, p. 3; 37 CFR § 1.192(c)5)(1993); now 37 CFR § 1.192(c)(7). Accordingly, we will limit our consideration of the issues raised in this appeal as they apply to claims 1, 4, 11, 22 and 46, which are representative of each ground of rejection. Claims 1 through 48 are attached as an appendix to this decision.

The references relied on by the examiner are:

Fillatti et al. (Fillatti), "Efficient Transfer of a Glyphosate Tolerance Gene into Tomato Using a Binary Agrobacterium Tumefaciens Vector," ***Bio/Technology***, Vol. 5, pp. 726-730, (1987).

Fitzgibbon, "**Pseudomonas** SP. Strain PG2982: Uptake of Glyphosate and Cloning of a Gene Which Confers Increased Resistance to Glyphosate," ***University Microfilms International***, pp. viii-ix, 18, 22-29, 32, 93 and 96-108, (1988).

Comai 4,769,061 Sep. 6, 1988

Potrykus, "Gene Transfer To Cereals: An Assessment," ***Bio/Technology***, Vol. 8, pp. 535-542 (1990).

DeGreve et al. (DeGreve) EPA 0 193 259 Sep. 3, 1986

The claims stand rejected as follows:[2]

[2] The Answer contains five additional rejections of the claims under the judicially-created doctrine of obviousness-type double patenting and 35 U.S.C. § 103. However, these rejection were withdrawn by the examiner in the Supplemental Answer (Paper No. 16).

I. Claims 1 through 7, 38 through 45 and 48 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention.

II. Claims 1 through 3 stand rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention.

III. Claims 1 through 4 and 6 through 47 stand rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to modifications of the sequences shown in Figure 1.

IV. Claims 22, 30, 38 through 41, 46 and 47 stand rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to dicot plants.

V. Claim 46 is rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is only enabling for claims limited to the modifications of the plant-derived sequences shown in Figure 1.

VI. Claims 11 through 14, 22 through 24 and 30 through 32 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Comai or Fillatti.

We affirm Rejections I and IV, and reverse Rejections II, III, V and VI.

Background and Discussion

The present invention is directed to a DNA sequence which encodes a novel 5-enolpyruvyl-3-phosphoshikimate (EPSP) synthetase enzyme, a method of making the DNA sequence, a plant cell transformed with said DNA sequence, a plant comprising said DNA sequence, a seed produced by a transformed plant, a method for producing glyphosate-tolerant plants, and a method for controlling weeds in a field containing crops. The novelty of the present EPSP enzyme is primarily due to two codon changes in a petunia-derived DNA sequence encoding said enzyme which result in the production of an enzyme having an alanine residue substituted for a glycine residue between amino acid positions 80 and 120 of the mature protein, and a threonine residue substituted for the terminal alanine, which is located between amino acid positions 170 and 210. According to the

specification, plants which are transformed with the altered EPSP gene are resistant to the herbicide N-phosphonomethylglycine (a.k.a., glyphosate).[3] The present invention is of agronomic importance since it enables farmers to control weeds in fields by spraying herbicides. Crop plants which comprise and express the altered gene (and, therefore, produce the altered enzyme) are protected from any detrimental effects dut to glyphosate.

Comai discloses a novel DNA sequence which encodes an EPSPS enzyme which is highly resistant to glyphosate. According to Comai, "the structural gene providing the glyphosate-resistant ES-3-P synthase [EPSPS] can be obtained as a mutation in the aroA gene of a glyphosate sensitive organism. ... The source of the aroA gene may be any organism which contains a functional aroA gene." Comai, col. 2, lines 31-33 and lines 39-40. Comai describes EPSP synthase enzymes wherein a proline residue has been substituted with a neutral aliphatic amino acid residue between amino acids 90 and 110. Comai, col. 3, lines 17-27. Comai states that "[o]f particular interest is the ***S. typhimurium***

[3] According to the specification, N-phosphonomethylglycine "is a non-selective, broad spectrum, postemergence herbicide which ... dissociates in aqueous solution to form phytotoxic anions. Several anionic forms are known. As used herein, the term 'glyphosate' refers to the acid and its anions." Specification, p. 1, lines 21-24.

gene, which has proline replaced by serine at amino acid 101 of the enzyme." Comai, col. 3, lines 33-35. Comai also discloses that the DNA sequence which encodes the glyphosate-resistant EPSPS enzyme can be used to transform a "wide variety of plants, both monocotyledon and dicotyledon." Comai, col. 7, lines 3-5. The transformed plants are resistant to herbicides which contain glyphosate.

Fillatti discloses a co-cultivation method for transforming tomato plants with a mutant ***aroA*** gene which confers resistance to glyphosate. Fillatti does not disclose the location, or types, of mutations in the ***aroA*** gene which are responsible for glyphosate tolerance but, instead, footnotes Comai as the source of the DNA sequence. Fillatti, p. 729, col. 2, lines 15-17 and endnote 6.

Fitzgibbon discloses the isolation of a DNA sequence derived from ***Pseudomonas*** sp. strain PG2982 which encodes an enzyme capable of conferring resistance to EPSPS (glyphosate). Since the isolated DNA sequence has (i) less than 40% homology with the ***aroA*** genes of ***E. coli*** and ***S. typhimurium,*** and (ii) the corresponding amino acid deduced from said DNA sequence has "no significant similarity to amino acid sequences of known proteins", Fitzgibbon acknowledges that the sequence does not

encode the ***Pseudomonas aroA*** gene. Fitzgibbon, pp. 32 and 96. Thus, Fitzgibbon concludes that expression of a resistant EPSPS gene may not be the only way to achieve glyphosate resistance. ***Id***. at p. 28, last para.

DeGreve discloses the use of genetic engineering techniques to transform plant cells and their progeny to express the Bt2 toxin derived from ***Bacillus thuringiensis***. According to DeGreve the successful transformation and expression of the Bt2 toxin may be more difficult than other genes for one or more reasons such as:

> (1) the large size of the Bt2 toxin, even in its truncated form; (2) the particular properties of the Bt2 polypeptide (such as, but not limited to, solubility of the polypeptide); (3) the potential toxicity of the Bt2 polypeptide toward the plant cells; or (4) the Bt2 polypeptide synthesized in plant cells and their progeny must retain substantially the same properties as the crystal protein synthesized in bacteria.

DeGreve, para. bridging pp. 3-4.

Potrykus provides a brief review of methods to produce transgenic cereals. According to Potrykus, it has not been generally possible to transform cereals (which are monocotyledonous plants)[4] using ***Agrobacterium*** as the vector.

[4] Potrykus notes that standard direct gene transfer (continued...)

Potrykus, p. 538, col. 2, para. 3; p. 540, col. 1, para. 3.

Potrykus prefaces his remarks with the statement that his

> assessment will be subjective. It will be based on a rigid definition of what constitutes ***proof*** of successful integrative transformation. Those who disagree with the view that indicative evidence is misleading may not agree with this assessment. The review will also be based on an interpretation of the biological factors affecting gene transfer, and several statements will be made for which no solid experimental data are available. (Emphasis in original.)

Potrykus, p. 535, col. 2, lines 9-21.

Rejection I

The examiner initially urges that the claims are unclear as to what the appellants intend by positions 80 and 120 and positions 170 and 210. The examiner states that "[i]t is confusing as to whether the numbering refers to amino acid or nucleic acid residues." Answer, p. 5, para. 3. We agree. We note the appellants attempt to rectify the problem in an amendment filed after the final office action, however, said amendment was not entered by the examiner.[5] Paper No. 10, mailed

[4](...continued)
procedures have been used to produce transgenic rice and maize plants. Potrykus, p. 540, col. 1, para. 3.

[5] The examiner refused entry of the amendment stating that "[a]lthough, substitution of 'enzyme' for 'gene' would have (continued...)

Oct. 16, 1992. Since we must consider the rejection as it applies to the claims before us, we ***affirm*** Rejection I.

Rejection II

The examiner states on p. 5, para. 5 of the Answer that:

> The recitation of claims 1-3 is confusing at [sic, as] these claims describe a product rather than a method. A straightforward reading of these claims would imply an in vitro modification of an EPSP synthase enzyme from a plant or bacterial source whereas the specification describes a process of mutagenesis of the corresponding nucleic acid sequence. Claim 1 should recite specific, active method steps which should include the essential nucleic acid intermediate.

In response the appellants argue that "[t]he examiner states that she is 'confused' about what claims 1-3 actually describe: either a product or a method. Applicants fail to understand the source of this confusion." And frankly, neither do we. That is, contrary to the examiner's remarks, we do not find that the method of making a gene as described in representative claim 1 to be directed to a product, or that the claim language in any

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[5](...continued)
removed one ground of rejection under 35 U.S.C. § 112, para. 2, other grounds of rejection would have remained." Advisory Action, Paper No. 12, p. 1. The examiner correctly pointed out that "[a]pplicants' amendment would change the last residue of the second amino acid sequence of claim 4 from T 6 A." ***Id.***

manner "implies an ***in vitro*** modification of an EPSP enzyme." Rather, § 112, second paragraph problems discussed above notwithstanding, we find that the claimed method is directed to the substitution of specific codons within specific regions of the EPSP synthase gene. The issue then to be resolved is whether the specification would have enabled one skilled in the art to make and use the claimed method. To that end the court in ***In re Marzocchi***, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) directs us to consider that "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented ***must*** be taken as in compliance with the enabling requirement of the first paragraph of § 112 ***unless*** there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." (Emphases in original.) In the case before us, the examiner acknowledges in the body of the rejection that the specification describes a process of mutating a DNA sequence which encodes an EPSP synthase enzyme. Answer, p. 5. She has not articulated any reasons as to why given this description one skilled in the art would have been unable to perform the claimed method. Accordingly, we find the

examiner has not met her burden of establishing a ***prima facie*** case of non-enablement.

In addition, we are puzzled as to the reason for the examiner's request that the claim recite specific method steps which include the nucleic acid intermediate(s). We are not aware of any case law which supports the examiner's position. To the contrary, both the statute and the court direct us, and the examiner, to determine whether the disclosure in the specification is sufficient to enable those skilled in the art to practice the claimed invention. ***Fiers v. Sugano***, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1607 (Fed. Cir. 1993) ("[e]nablement requires that the application 'contain a description that enables one skilled in the art to make and use the claimed invention,'" quoting ***Atlas Powder Co. V. E.I. duPont De Nemours & Co.***, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984)); ***United States v. Telectronics, Inc.***, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), ***cert. denied*** 490 U.S. 1046 (1989); ***In re Wands***, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); ***In re Vaeck***, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). At best, this aspect of the rejection is a remnant of the § 112, second paragraph discussed above. However, having already

affirmed this rejection with respect to claims 1 through 3, we decline to do so again. Accordingly, we direct attention to our disposition of the § 112, second paragraph issue above, although we ***reverse*** Rejection II, in its entirety.

Rejection III

The examiner urges that the specification is enabling only for "the sequences shown in Figure 1 (see Fitzgibbon). Consequently, there is no guidance such that one skilled in the art would know where to make the appropriate mutations . . . one could not predict that application of the mutations in the regions claimed to any EPSPS encoding sequence would yield an effective glyphosate tolerant gene and corresponding plant." Answer, p. 6. We find this position untenable.

The enablement section of 35 U.S.C. § 112, first paragraph, "requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." ***In re Fisher***, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Thus, in order to determine whether the present claims are enabled, we must analyze the teachings of the specification, and make an inquiry into the knowledge of persons of ordinary skill in the

art. ***In re Bowen***, 492 F.2d 859, 861, 181 USPQ 48, 50 (CCPA 1974). Here, we find that the specification teaches those skilled in the art how to make the claimed codon substitutions within the EPSPS DNA sequence by site-directed mutagenesis. Specification, pp. 51-54. Moreover, as pointed out by the appellants, the specification (Figure 1) also provides teachings as to the types of plant and bacterial species contemplated by their invention. Brief, p. 19. These points are not refuted by the examiner; rather, she alleges that additional DNA sequences are within the scope of the claim and if those skilled in the art wanted to make the claimed codon substitutions using DNA sequences which do not have the consensus sequence set forth in Figure 1, s/he could not do so following the techniques described in the specification. The examiner's analysis is improper. As held by the court in ***In re Borkowski***, 422 F.2d 904, 909, 164 USPQ 642, 645 (CCPA 1970), it is inappropriate "to study appellants' disclosure, to formulate a conclusion as to what he (the examiner) regards as the broadest invention supported by the disclosure, and then to determine whether appellants' claims are broader than the examiner's conception of what 'the invention' is." Therefore, in the case before us since the techniques disclosed in the specification only employ DNA sequences which

encode the consensus amino acid sequences in the specified locations for use in the claimed process, then those DNA sequences, such as that which is disclosed by Fitzgibbon, are not within the scope of the claim. That is to say, in our opinion, representative claim 1 is limited to the EPSPS sequences which encode the consensus amino acid sequences set forth in Figure 1.

Accordingly, Rejection III is ***reversed***.

Rejection IV

The examiner argues that the specification "is only enabling for dicot plant species." Answer, p. 6. According to the examiner, "[e]xtrapolation to other species from Applicants' specification would require undue experimentation by one skilled in the art because methods of transformation and regeneration are not generally available for monocot species (see Potrykus)." ***Id***.

It is well established that the examiner may reject the claims as being based on a non-enabling disclosure when s/he has reason to conclude that one skilled in the art would be unable to carry out the claimed invention. ***In re Buchner***, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Here, we find that the examiner has such reasons based on the disclosure of Potrykus that the transformation of monocotyledonous plants, except for

maize and rice, "is likely to be a problem for some years because, so far, the establishment of the appropriate cell cultures is an art that depends upon parameters beyond experimental control (Potrykus, page 540, section 12)." Answer, sentence bridging pp. 17-18. Having provided objective evidence to support her position, the burden now shifts to the appellants to demonstrate by way of rebuttal evidence that the application is enabling. ***In re Marzocchi***, 439 F.2d at 223, 169 USPQ at 369.

In their response, however, the appellants address the rejection only as it applies to claim 46. Brief, p. 21. The appellants contend that "suitable transformation methods for both dicot and monocot plants were known at the time of filing of the instant application" and they refer generally to a list of references provided in an amendment, filed December 11, 1991 (Paper No. 5). Brief, p. 21, lines 4-8. In addition, the appellants argue that the teachings on pp. 66-68 of the specification demonstrate that techniques known in the art were used for the regeneration of maize protoplasts which expressed the claimed variant EPSPS. Thus, the appellants urge that it would not require undue experimentation for one skilled in the art to make and use the invention described in claim 46. We find the appellants' position untenable.

It is well established that § 112, first paragraph, requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. ***In re Fisher***, 427 F.2d at 839, 166 USPQ at 24. The court recognizes that patent applicants are not required to disclose that which is well known in the art,[6] however, the specification must "teach those of ordinary skill how to make and use the invention as broadly as it is claimed." ***In re Vaeck***, 947 F.2d at 496, 20 USPQ2d at 1445. The court has cautioned that "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." ***Genentech, Inc. v. Novo Nordisk A/S***, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997).

To that end, we turn to the description of maize protoplasts on pp. 66-68 of the specification. As we understand it, the teachings in the specification are prophetic with respect to the production of transgenic maize plants which express the claimed EPSPS variant. Thus, given the problems of making transgenic cereals as described by Potrykus, it is not clear whether the

[6] ***See, e.g., Hybritech, Inc. V. Monoclonal Antibodies, Inc.***, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986), ***cert. denied***, 480 U.S. 947 (1987).

specification disclosure would have enabled one skilled in the art to make transgenic maize. We need not make this determination, however, because we do not find the single, disclosed example of maize protoplasts which express the variant EPSPS sufficient to enable the one skilled in the art to make the invention as broadly claimed. That is, the method of claim 46 encompasses all monocot plant species. However, Potrykus discloses that in 1990, the filing date of the present application, standard direct gene transfer procedures, were not generally applicable to all monocots, but had only been successful with maize and rice. Thus, on these facts, we find that successful results obtained for the regeneration of transformed maize protoplasts do not enable those skilled in the art to practice the full scope of the invention, absent undue experimentation. ***In re Goodman***, 11 F.3d 1046, 1050, 29 USPQ2d 2010, 2013 (Fed. Cir. 1993), citing ***In re Wands***, 858 F.2d at 737, 8 USPQ2d at 1404.

As to the list of reference titles submitted by the appellants, we are unable to discern on the basis of this information alone, what was known in the art with respect to the production of transgenic cereals at the time the application was filed. Absent the references themselves, it is not possible to

determine whether those skilled in the art could practice the method of claim 46 without undue experimentation. Moreover, we also note from the titles of the articles that they appear to be directed to the two exceptions taught by Potrykus, i.e., rice and maize.

Thus, from the evidence of record, we conclude that since the scope of claim 46 includes all monocotyledonous plants, the appellants have failed to meet their burden of establishing that the specification provides an enabling disclosure.[7] ***Genentech Inc. v. Novo Nordisk A/S***, 108 F.3d at 1366, 42 USPQ2d at 1005 ("Tossing out the mere germ of an idea does not constitute enabling disclosure").

[7] We direct attention to the enablement issue raised in ***Goodman*** as to whether or not the specification would have enabled one skilled in the art to produce any type of mammalian peptide by transforming any type of plant cell, which includes monocot plants, with a structural gene encoding a desired peptide. ***In re Goodman,*** 11 F.3d at 1050-1052, 29 USPQ2d at 2013-2015. The court concluded from the art of record that because the methods of transforming monocot plants were unreliable and unpredictable, it would have required "extensive experimentation to practice the claimed method for just a few plants, let alone all plant cells as broadly claimed in the application." ***Id.*** at 1052, 29 USPQ2d at 2015. We acknowledge that the filing date of the present application is five years later than the filing date of the ***Goodman*** application, however, the appellants have failed to provide any evidence that the art of transforming monocot plants with DNA sequences encoding heterologous proteins of interest, and the subsequent expression of said proteins, has advanced during the intervening time period.

Since the appellants have failed to meet their burden of establishing that the specification enables the method of claim 46, and they have offered no rebuttal evidence with respect to claims 22, 30, 38-41, and 47, we are constrained to affirm the rejection.

Rejection IV is ***affirmed***.

Rejection V

The examiner argues that the specification fails to enable claim 46 "because expression of a foreign gene in a plant, especially when the gene is of procaryotic origin, is unpredictable." The examiner relies on the teachings of DeGreve to support her position. We disagree.

Since claim 46 contains the same amino acid sequence limitations as claim 1, we find for the reasons discussed for Rejection III above, that it is limited to EPSPS sequences which encode the consensus amino acid sequence set forth in Figure 1.

As to the examiner's argument that the expression of the claimed EPSP variants in plants is unpredictable, we find her reliance on the teachings of DeGreve to be misplaced. DeGreve describes problems which are specific to the expression of a different protein (Bt2 toxin). These problems are due to the

particular properties, size and potential toxicity of Bt2 toxin and, absent evidence to the contrary, they are not relevant to the expression of the claimed EPSPS sequences.

Accordingly, Rejection V is ***reversed***.

Rejection VI

The examiner argues that the claims directed to transformed plant cells, plants, and their seed are not patentable over the glyphosate resistant plants taught by Comai or Fillatti. The examiner acknowledges on p. 7 of the Answer that

> the genome of Applicants' claimed plants, seeds, and plant cells may differ from the genome of the glyphosate resistant plants of Comai or Fillatti, et al, the prior art plants and plant cells would be indistinguishable from the claimed plants with respect to physical characteristics. Applicants do not provide any evidence that the glyphosate tolerant plants transformed with a gene containing the specific mutations cited performs [sic, perform] any differently than glyphosate tolerant plants known in the art such as those taught by Comai and Fillatti et al.

In the alternative the examiner urges on p. 8 of the Answer that:

> If, in fact, the claimed and reference [sic, referenced] plants are not identical, then the existence of glyphosate resistant plants would reasonably have suggested the existence of the same or similar products to one of ordinary skill in the art, making the claimed invention as a whole ***prima facie*** obvious to those of ordinary skill in the art at the time the claimed invention was made.

In their response the appellants point out that although Fillatti does not describe the EPSPS variant used in the studies, the evidence of record indicates that their variant was obtained from Comai. Therefore, the appellants conclude that the EPSPS variant employed by Fillati is the same as the variant taught by Comai. Brief, p. 24, para. 1. The examiner does rebut the appellants' finding, thus, for purposes of this appeal, we will assume that the EPSPS variants disclosed by Fillatti and Comai are identical.

We greatly appreciate the examiner's concerns that phenotypically there may be no differences between the claimed glyphosate-resistant plants and those of the prior art. ***In re Best***, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) (Where the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product). However, in the case before us, the claimed variants contain two different mutations in two different regions of the nucleotide/amino acid sequences. The mere fact that claimed mutations are in the same EPSPS enzyme as the prior art, does not

necessarily indicate that present variants will have the same enzyme specificity as the prior art variants. In our view, since there are amino acid substitutions in two separate, conserved regions of the EPSPS enzyme, it is reasonable to expect the K_m of the claimed variant to differ from that of the prior art. We point out that inherency must be based on inevitability, not speculation. ***In re Oelrich***, 666 F.2d 578, 581-582, 212 USPQ 323, 326 (CCPA 1981). Since the examiner has not given any reasons as to why the plants comprising the instant EPSPS enzyme variants would be expected to have the same glyphosate-resistant phenotype as the plants taught by Comai and Fillatti, we find that the examiner's conclusion is based on speculation.

As to the obviousness of the present variants over the prior art, we agree with the appellants that the applied prior art fails to provide any teaching or suggestion of the claimed mutations. Given that there are a myriad of possible mutations within the EPSPS enzyme, there must have been some suggestion in the applied prior art to make the claimed variants in order to establish a ***prima facie*** case of obviousness. The examiner has failed to provide any evidence of such a suggestion either in applied prior art or on the basis of knowledge generally

available to those of ordinary skill in the art. ***In re Fine***, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

Accordingly, Rejection VI is ***reversed***.

The decision of the examiner is affirmed-in-part.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

WILLIAM F. SMITH Administrative Patent Judge	)	
TEDDY S. GRON Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
JOAN ELLIS Administrative Patent Judge	)	

Appeal No. 93-2460
Application No. 07/590,647

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JE/jrg

APPENDIX

1. A method for producing a gene encoding a glyphosate-tolerant 5-enolpyruvyl-3-phosphoshikimate (EPSP) synthase enzyme which comprises substituting, in a EPSP synthase gene encoding a protein containing the amino acid sequences shown below located in the indicated positions, a codon encoding an alanine residue for the second glycine residue in a first amino acid sequence:

-L-G-N-A-G-T-A-

located between positions 80 and 120 in the EPSP synthase gene, and further substituting a codon encoding a threonine residue for the codon encoding the terminal alanine residue in a second amino acid sequence:

-A-L-L-M-X_1-A-P-L-A-

where X_1 is either alanine, serine or threonine, and where said second amino acid sequence is located between positions 170 and 210 in the EPSP synthase gene.

2. A method of Claim 1 in which the glyphosate-tolerant EPSP synthase gene is produced from a plant EPSP synthase gene.

3. A method of Claim 1 in which the glyphosate-tolerant EPSP synthase gene is produced from a bacterial EPSP synthase gene.

4. A gene encoding a glyphosate-tolerant 5-enolpyruvyl-3-phosphoshikimate (EPSP) synthase enzyme which encodes a first amino acid sequence:

-L-G-N-A-A-T-A-

between positions 80 and 120 in the EPSP synthase gene, and encodes a second amino acid sequence:

-A-L-L-M-X_1-A-P-L-T-

where X_1 is either alanine, serine or threonine, where said second amino acid sequence is located between positions 170 and 210 in the EPSP synthase gene.

5. The gene of Claim 4 encoding a protein as shown in Figure 1 but which protein contains the first and second amino acid sequences.

6. A gene encoding a glyphosate-tolerant EPSP synthase produced by the method of Claim 1 wherein the EPSP synthase gene in which the codon substitutions are made is selected from the group of EPSP synthase consisting of petunia, tomato, maize, *Arabidopsis thaliana,* soybean, *Brassica napus, E. coli* K-12, and *Salmonella typhimurium* proteins as shown in Figure 1.

7. A plant gene encoding a glyphosate-tolerant EPSP synthase enzyme of Claim 4.

8. A plant transformation vector comprising a gene which encodes a glyphosate-tolerant 5-enolpyruvyl-3-phosphoshikimate (EPSP) synthase having a first amino acid sequence:

-L-G-N-A-A-T-A-

located between positions 80 and 120 of the mature EPSP synthase sequence and a second amino acid sequence

-A-L-L-M-X_1-P-L-T-

wherein X_1 is either alanine, serine or threonine, where said second amino acid sequence is located between positions 170 and 210 in the mature EPSP synthase sequence.

9. A vector of Claim 8 containing a glyphosate-tolerant plant EPSP synthase.

10. A vector of Claim 8 containing a glyphosate-tolerant bacterial EPSP synthase.

11. A transformed plant cell containing a gene of Claim 7.

12. A transformed plant cell of Claim 11 selected from the group consisting of tomato, tobacco, oil seed rape, flax, soybean, sunflower, sugar beet, alfalfa, cotton, rice and maize.

13. A transformed cell of Claim 11 from tomato.

14. A transformed cell of Claim 11 from tobacco.

15. A transformed cell of Claim 11 from oil seed rape.

16. A transformed cell of Claim 11 from flax.

17. A transformed cell of Claim 11 from soybean.

18. A transformed cell of Claim 11 from sunflower.

19. A transformed cell of Claim 11 from sugar beet.

20. A transformed cell of Claim 11 from alfalfa.

21. A transformed cell of Claim 11 from maize.

22. A plant comprising transformed plant cells of Claim 11.

23. A plant of Claim 22 in which the plant is tomato.

24. A plant of Claim 22 in which the plant is tobacco.

25. A plant of Claim 22 in which the plant is oil see rape.

26. A plant of Claim 22 in which the plant is flax.

27. A plant of Claim 22 in which the plant is sunflower.

28. A plant of Claim 22 in which the plant is sugar beet.

29. A plant of Claim 22 in which the plant is alfalfa.

30. A seed produced by a plant of Claim 22.

31. A seed of Claim 30 in which the plant is tomato.

32. A seed of Claim 30 in which the plant is tobacco.

33. A seed of Claim 30 in which the plant is oil seed rape.

34. A seed of Claim 30 in which the plant is flax.

35. A seed of Claim 30 in which the plant is sunflower.

36. A seed of Claim 30 in which the plant is sugar beet.

37. A seed of Claim 30 in which the plant is alfalfa.

38. A method for producing glyphosate-tolerant plants which comprises propagating a plant containing a plant gene of Claim 4.

39. The method of Claim 38 in which the propagated plant is selected from the group consisting of maize, tomato, tobacco, oil seed rape, flax, sunflower, sugar beet, alfalfa, cotton, and rice.

40. A method of Claim 38 in which a first plant is propagated by crossing between said first plant and a second plant, such that at least some progeny of said cross display glyphosate tolerance.

41. A method of Claim 40 in which the plant is selected from the group consisting of maize, tomato, tobacco, oil seed rape, flax, sunflower, sugar beet, alfalfa, cotton and rice.

42. A DNA sequence encoding a glyphosate-tolerant EPSP synthase of Claim 4.

43. A DNA sequence of Claim 42 which is less than twenty kilobases in length.

44. A DNA sequence of Claim 43 encoding a glyphosate-tolerant plant EPSP synthase.

45. A DNA sequence of Claim 43 encoding a glyphosate-tolerant bacterial EPSP synthase.

46. A method for selectively controlling weeds in a field containing a crop having planted crop seeds or plants comprising the steps of:

planting said crop seeds or plants which are glyphosate tolerant as a result of containing a gene encoding a glyphosate-tolerant EPSP synthase enzyme which contains the amino acid sequence -L-G-N-A-A-T-A- between positions 80 and 120 in the mature EPSP synthase sequence, and a second amino acid sequence -A-L-L-M-X_1-A-P-L-T-, where X_1 is either alanine, serine or threonine, and where said second amino acid sequence is located between positions 170 and 210 in the mature EPSP synthase sequence; and

applying to said crop and weeds in said field a sufficient amount of glyphosate to control said weeds without significantly affecting said crop.

47. The method of Claim 46 wherein said gene encoding a glyphosate-tolerant EPSP synthase enzyme is from a plant source.

48. The method for producing a gene of Claim 1 which comprises making the indicated codon substitutions in a EPSP synthase gene encoding a protein of Figure 1.

APPEAL NO. 93-2460 - JUDGE ELLIS
APPLICATION NO. 07/590,647

APJ ELLIS

APJ W. SMITH

APJ GRON

DECISION: AFFIRMED-IN-PART

Typed By: Jenine Gillis

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